REMARKS

Claims 1- 24 are pending. Further to the telephone conversation of December 18, 2002 between the Examiner and Applicants' representative Jeffrey D. Hsi, Applicants affirm the election of restriction Group I, including claims 1-17. As such, claims 18-24 stand withdrawn as being drawn to a non-elected invention.

Applicants have amended claims 1, 5, and 16. Support for these amendments appears throughout the specification and claims as originally filed, including at page 9, line 23 and original dependent (from claim 1) claim 5 (halogen) and page 10, line 13, and original dependent (from claim 1) claim 11 (solvate). No new matter is introduced by these amendments. Applicants make these amendments in order to expedite prosecution of these claims and to comport the claims with the elected subject matter. Applicants make such amendments without prejudice to pursuing the originally presented or cancelled subject matter in a later application claiming benefit of this application, and particularly without prejudice to determination of equivalents of the subject matter of this application or any later application claiming benefit of this application.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-17 are rejected as being indefinite for multiple reasons delineated below.

It is alleged in the Action that the phrase "protecting groups" in claim 1 (and claims 2-17 thereby as they depend from claim 1) is unclear as to what groups are contemplated. Applicants traverse. While Applicants' have amended claim 1 to recite specific groups (i.e., t-BOC, benzyl and trityl) in order to expedite prosecution, thus rendering the rejection moot, Applicants submit that one of ordinary skill reading the specification (and references in the art including Greene referenced at page 12, lines 7-9 of the specification) would be in a position to contemplate the groups delineated as "nitrogen-protecting groups". Applicants reserve for future prosecution in applications claiming benefit of the instant application their ability to forward this position without prejudice.

It is also alleged that the terms "aryl" and "heteroaryl", as they each use the word "includes" (thus leaving the definition open to the inclusion of other rings) is indefinite. Applicants traverse. Applicants submit that one or ordinary skill in the art would understand the meanings of those terms when read in the context of knowledge in the art and the specification. The term "aryl" is understood by one of skill in the art to mean an aromatic hydrocarbon ring system, which may be one or more rings, of which phenyl, 1-naphthyl, and 2-naphthyl are all examples. The term "heteroaryl" is understood by one of skill in the art to mean an aromatic hydrocarbon ring system having at least one heteroatom (e.g., O, N, or S) in the ring system, of which pyrrole, imidazole, thiophene, furan, ... etc. are all examples. Based on the foregoing reason, Applicants request withdrawal of this rejection.

It is further alleged that the "nature of intended rings formed at NR5R6 is not adequately set forth" (the Office Action, page 5, section 3). Applicants traverse. Claim 1 recites that "R5 and R6 together with the nitrogen atom to which they are bound form a saturated heterocyclic ring having 4-7 ring members which ring may contain an additional heteroatom and which may be substituted by methyl, oxo, or hydroxy." One of ordinary skill in the art would understand what a saturated heterocyclic ring is, and further, when reading the exemplary heterocyclic rings provided in the specification (page 10, lines 16-18), would appreciate the nature of the recitation. Applicants point to a variety of basic chemistry treatises, including for example, S.N. Eğe, *Organic Chemistry*, D.C. Heath and Company, Lexington Massachusetts, (1984), a textbook typical of those used in introductory university courses in chemistry. Applicants submit pages 1009 to 1011 of Eğe, *Organic Chemistry*, to support this proposition. Page 1011 of Eğe, in particular, describes and provides examples of saturated heterocyclic groups. As shown by Eğe and other similar treatises in the field, one of ordinary skill would understand the concept of the ring system described by NR5R6 in Applicant's claims. Based on the foregoing reasons, Applicants request withdrawal of this rejection.

It is also alleged that "the scope of 'prodrug forms' is completely unknown ... Specification provides no guidance" (the Action, page 5, section 4). Applicants traverse.

The term "prodrug" is a well accepted and understood term, both in the art and in issued U.S. Patents in the art. The term "prodrug" is specifically supported by the definition at page 11, lines 12-16 of the specification, as well as in the cited reference (Goodman) therein. Moreover, a

search of the U.S. Patent Office database identified at least 808 issued U.S. Patents that have claims containing the language "prodrug". U.S. Patent Nos. 6,310,080 and 6,310,075, which were randomly selected for review, recite the term "prodrug" in the claims, however, in US 6,310,080 there is no explicit definition whatsoever of the term in the specification and in US 6,310,075 (see, column 16, line 60 to column 17, line 15) there is merely a general definition that is commensurate with that contained in Applicants' specification and also with that of the Goodman reference, cited in Applicants' specification to illustrate the state of the art.

The term "prodrug forms" is clearly defined in the specification (page 9, lines 3-4), and the Goodman and Gilman reference, "The Pharmacological Basis of Therapeutics", which is incorporated by reference (page 9, lines 5-6) and describes prodrugs. Applicants also submit "The Organic Chemistry of Drug Design and Drug Action" Richard B. Silverman. Chapter 8, p 352. (Academic Press, Inc. 1992. ISBN 0-12-643730-0). (Appendix 2; p. 352, 1st paragraph, 1st sentence), as support for the state of the art. In view of the definition in Applicants' specification as well as the Goodman and Gilman book, and the knowledge of one of ordinary skill in the art (including Silverman), Applicants submit that one of ordinary skill would be able to determine the scope of the claimed subject matter.

Based on the foregoing, Applicants submit it is well within the knowledge of one of ordinary skill in the art, of what is deemed to be a "prodrug" and therefore that term is not indefinite. Applicants request that this rejection be withdrawn.

Claim 11, dependent from claim 1, is rejected on the ground that it recites "solvates" while claim 1 recites "hydrates" (the Action, page 6, section 5) and thus is outside the scope of claim 1. Applicants have amended claim 1 to recite "solvates". Support for this amendment appears throughout the specification and claims as originally filed, including at page 10, line 13. Applicants note that hydrates are a subset of solvates.

Method claims 13, 14, and 17 are rejected for several reasons, e.g., (i)"no one particular disorder is recited"; (ii) "how does one determine who is in need and who is not"; (iii) "[t]o what other serotonin receptors are the instant compounds capable of binding"; (iv) "what interaction qualifies as 'modulating' ?"; (v) "what success rate determines if a particular inhibitor is effective,

how many patients (and dosage regimens) need be tested?" (See, Action, page 6, section 6). Applicants traverse.

In this regard to (i) above, it is the Examiner's position that since no particular disorder is recited, the claim is indefinite. Applicants disagree. Applicants submit that a skilled person in the art, in light of the specification and teachings of the prior art, would be apprised of the claim scope. The method claims relate to disease where serotonin is involved, including $5HT_{2c}$ receptor binding. The meaning is clear, any disease in which serotonin, including $5HT_{2c}$ receptor binding, is involved. The concept is not indefinite. One of ordinary skill is able to ascertain whether 5-HT2c receptor binding is involved in the disease pathology, by knowledge of the relevant literature and state of the art as well as studies described in the specification as filed (including those cited at page 10, lines 20-30) and including references delineated for the specific diseases below as well as general review articles in the field also delineated below.

Specific diseases are known and readily identifiable, as shown by art, including that cited by the Examiner, as well as references specifically delineated below. Moreover, Applicants submit an article by Fitzgerald and Ennis entitled "5-HT_{2c} Receptor Modulators: Progress in Development of New CNS Medicines", *Annual Reports in Medicinal Chemistry*, (37), page 21 (2002), which although published later than Applicants' filing date, nonetheless confirms the role of 5-HT_{2c} receptors in therapy delineated in Applicants' specification as filed.

In regard to (ii) above, one who is "in need" of treatment can be identified by a number of ways, and this would be in the purview of one of ordinary skill in the art. Typically, one of skill in the art would understand that the determination could be by the subject (e.g., subject feels they need treatment for a disease or disease state) or by a health care provider. In reality, one of skill in the art would understand that such determination would be under the auspices of a health care provider (e.g., physician) and ultimately under the auspices of a regulatory agency, (e.g., the U.S. Food and Drug Administration ("FDA")). As such, Applicants submit that one of ordinary skill in the art, reading Applicants' specification, would understand such "determination" aspects of the claimed methods. However, Applicants note that while for such a determination FDA authority would ultimately guide the method, that is separate and distinct from applying FDA standards of safety and efficacy to the context of patentability. That is, while one of ordinary skill in the art would understand that FDA teachings would guide such determinations, that does

not mean that it is appropriate for the Patent Office to impose FDA drug evaluation criteria to determine patentability.

In regard to (iii), method of making and using the instant compounds, as delineated in the specification, are established. Furthermore, as stated in the specification, one of ordinary skill would be enabled to screen the instant compounds against any of a number of serotonin targets. Such screens are known in the art, including those delineated in Gaster, as well as the other references submitted herewith.

In regard to (iv), the term "modulating" includes both agonism and antagonism. This is apparent from a reading of the specification throughout, and including specifically at page 8, first paragraph, where the compounds of the instant invention are described as "5-HT_{2c} receptor agonists and antagonists." If it is being alleged in the Action that the language is indefinite because it is counterintuitive that a specific compound can simultaneously have agonistic and antagonistic activity, Applicants are willing to amend the specification at page 8, first paragraph of the specification, which refers to the group of all compounds of formula I taken as a group having antagonist "and" antagonist activity; to read agonist "or" antagonist activity. Applicants submit, however, that one of ordinary skill would understand that such a phrase means that each individual compound can only be either an agonist or an antagonist as one of ordinary skill would understand the definitions of the two terms to be mutually exclusive (that is, a compound binding to a receptor either elicits a functional activity or does not).

In regard to (v), Applicants submit that the queries at paragraph 6, lines 7-12 regarding "% effectiveness" and "success rate" are not proper standards by which to assess patentability. As mentioned above, criteria used by a regulatory agency (e.g., the FDA) to establish safety and efficacy of a drug for human therapy are separate and distinct from criteria used to assess patentability. MPEP 2107.03. As stated above, one of ordinary skill would understand, both from reading the specification (e.g., dosage regimens as described at page 14, lines 6-18 of the specification) and guidance ultimately from a healthcare provider (e.g., treating physician, pharmacist) and ultimately under the auspices of the FDA as determined from clinical trial studies, what the range of effective amounts would be. As such, Applicants submit that one of ordinary skill in the art is placed in a position to understand the practice of the methods of claims 13, 14 and 17 on the basis of the knowledge possessed by one of ordinary skill at the time of

NA asking for clinical efficacy

filing as well as Applicants' specification. Applicants have discovered that compounds of their invention are useful in modulating the 5-HT_{2c} receptor, which has implications for treating disease states. One of ordinary skill, in light of Applicants' specification, would understand whether the 5-HT_{2c} receptor is involved in disease pathology and understand how to practice the method as claimed. For these reasons, Applicants request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-17 are rejected as containing subject matter not described in such a way as to enable one skilled in the art to make or use the invention.

(1) Pyrazines

It is alleged that Applicants have not enabled the scope of pyrazines claimed, and further, that only five compounds have been prepared and only two tested for 5-HT_{2c} activity. Applicants disagree.

The law on this matter is clear. The standard for enablement is not the number of examples cited in the specification: rather, the standard is whether one of ordinary skill in the art, in light of the written description, would be capable of making and using the invention. One is not required to provide a complete and fully comprehensive exposé of every variation and nuance of the invention. In fact, experimentation that is routine or repetitious, even if lengthy, is permissible. "[A] considerable amount of experimentation is permissible, if it is merely routine..." *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (CAFC 1988), citing *In re Jackson*, 217 USPQ 804, 807 (Bd. App. 1982). It is clear that making and testing a compound delineated in Applicants' claimed formula would be routine in view of the guidance provided in the specification and the teachings of the art (including making, using, and screening), and no evidence to the contrary is identified in the Action. While potentially lengthy, such work would, in fact, be routine and repetitious.

Note that it is not necessary for Applicants to make or test all species covered by a generic claim to show their operativeness (although as seen in the specification, [insert if anything]). The law does not impose such a formidable burden on inventors seeking patent protection, as "appellants (here, Applicants) are not required to disclose every species

encompassed by their claims even in an unpredictable art" (parentheses added). *In re Angstadt*, 537 F.2d 498, 503, 190 USPQ 214, 218 (CCPA 1976). Such a holding is only reasonable, as it would be onerous, if not impossible, to test and disclose all operative species in the chemical and biotechnology fields. Moreover, to require so would apparently necessitate a patent application with an enormous number of working examples. As the Angstadt court explains:

> such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid 'literal' infringement of such claims by merely finding another analogous catalyst complex (here, another derivative compound of the delineated formula) which could be used in 'forming hydroperoxides' (here, compounds of the delineated formula). *Id.* at 503, 190 USPQ at 218 (parentheses added).

The assertions forwarded in the Action (e.g., "the level of unpredictability" and "lack of direction (i.e., working examples") are generalizations and are unsupported by any stated evidence. Applicants' claims relate to compounds and methods of using them for 5-HT2c receptor function and treating disease related to the 5-HT2c receptor. Applicants have delineated in their specification guidance and examples of making and using compounds that inhibit 5-HT2c receptor function. Applicants also submit that other compounds of formula I in claim 1 have shown binding in the assays described in their specification. Applicants also make reference to dosage levels in their specification (see, page 14, lines 6-18). One of ordinary skill in the art would: 1) find sufficient working examples of 5-HT2c inhibitor compounds in Applicants specification; 2) based on a combination of ordinary skill in the art as well as Applicants' disclosure of methods for determining 5-HT2c inhibition activity, find sufficient skill to make and determine 5-HT2c inhibitor compounds; and 3) find predictability for methods of inhibiting 5-HT2c receptor (and disease mediated thereby) based on immutable showings of 5-HT2c inhibition activity of Applicants' compounds and uses thereof as demonstrated in the examples in Applicants' specification. In short, nowhere in the Action is evidence (other than conclusory assertions) provided that is contrary to that provided as written description in Applicants' specification.

Additionally, it is alleged that Applicants own statement at page 19 of their specification (that "for exemplary compounds of the invention the range in activity varied as much as 1500-fold") evidences the structure-sensitivity of receptor binding. Applicants disagree with this misinterpretation. Whether 1 nm or 1500 nm, the compounds have inhibitory activity and everything in this range is enabling. Thus, the compounds have inhibitory activity and the Examiner has not provided any evidence to the contrary. Moreover, no evidence is provided in the Action to support a position that any compound, whether inhibitory at 1 nm or 1500 nm (that is, 1.5 μm), is necessarily not useful. It appears that it is being alleged that such a range of activity evidences unpredictability of structure-activity relationship and is therefore not enabling. This is misguided. One of ordinary skill in the art would appreciate that any compound over such a range of activity (or even higher) could potentially serve as a therapeutic.

Based on the foregoing, Applicants submit that the specification as filed enables one of ordinary skill to make and use the invention (i.e., pyrazines of the formula) and request that this rejection be withdrawn.

(2) Solvates

It is alleged in the Action that "solvates" are not enabled since "generally not all solvents can form solvates with all compounds." Applicants disagree. First, no evidence is provided in the Action to support the proposition that "generally not all solvents can form solvates with all compounds." Second, Applicants submit that one of ordinary skill would appreciate how to make a solvate of the instant compounds. In fact, this would typically be done by taking an instant compound up in a solvent of choice, and removing the excess solvent; leaving the solvate. Even, *arguendo*, if the statement "generally not all solvents can form solvates with all compounds" were true, that is not in and of itself a basis for finding nonenablement. As stated above, "[A] considerable amount of experimentation is permissible, if it is merely routine..." *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (CAFC 1988), citing *In re Jackson*, 217 USPQ 804, 807 (Bd. App. 1982). It is clear to one of ordinary skill in the art that making and testing a solvate of a compound delineated in Applicants' claimed formula would be routine in view of the guidance provided in the specification and the teachings of the art (including making,

using, and screening), and no evidence to the contrary is identified in the Action. As such, Applicants request withdrawal of this rejection.

(3) Prodrugs

It is alleged that "no reasonable assurance that any and all 'prodrug' derivatives of instant compounds will have ability to generate the instant compounds in vivo by one or more processes." Applicants disagree.

The rejection is founded on a basis that is unsupported by fact or law. Applicants have exemplified the use of various "prodrug" forms, including those delineated in the claims. One skilled in the art, reading Applicants' specification, would have no trouble whatsoever making and using the invention as claimed (i.e., methods of treating or preventing 5-HT2c receptor diseases by administering 5-HT2c receptor inhibitors). In response to the assertion in the Action that Applicants provide no reasonable assurance that the derivatives of the instant compounds (i.e. prodrugs) will have the ability to generate compounds in vivo, Applicants point out that a "prodrug", by definition, must inherently be one that is metabolized to the compound at issue. Thus, the question of whether or not a "prodrug" will have the ability to generate the instant compounds *in vivo* (Action at page 8, paragraph number 3) is irrelevant, because a "prodrug" by definition must generate the instant compound. Further, nowhere in the Action is any evidence cited that provides support for a position contrary to Applicants' teaching. Indeed, no rationale is provided for the rejection other than general, and unsupported, statements of unpredictability and disbelief. No reference is made to any teaching that is contrary to that of Applicants' claimed subject matter.

The law on this matter is clear. The standard for enablement is not the number of examples cited in the specification: rather, the standard is whether one of ordinary skill in the art, in light of the written description, would be capable of making and using the invention. One is not required to provide a complete and fully comprehensive exposé of every variation and nuance of the invention. In fact, experimentation that is routine or repetitious, even if lengthy, is permissible. **"[A] considerable amount of experimentation is permissible, if it is merely routine..."** *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (CAFC 1988), citing *In re Jackson*, 217 USPQ 804, 807 (Bd. App. 1982). It is clear that making and testing a prodrug of

any compound delineated herein would be routine in view of the guidance provided in the specification and the teachings of the art (including Goodman), and no evidence to the contrary is identified in the Action. While potentially lengthy, such work would, in fact, be routine and repetitious.

Note that it is not necessary for Applicants to make or test all species covered by a generic claim to show their operativeness The law does not impose such a formidable burden on inventors seeking patent protection, as "appellants (here, Applicants) are not required to disclose every species encompassed by their claims even in an unpredictable art" (parentheses added). *In re Angstadt*, 537 F.2d 498, 503, 190 USPQ 214, 218 (CCPA 1976).

The assertions forwarded in the Action (e.g., " 'sufficient working examples', 'the level of skilled in the art', and 'predictability', etc. have been demonstrated to be sufficiently lacking...") are generalizations and are unsupported by any stated evidence. Applicants' methods claims relate to 5-HT2c receptor function and disease related to the 5-HT2c receptor. Applicants have delineated in their specification numerous how to practice the claimed methods. One of ordinary skill in the art would: 1) find sufficient working examples of 5-HT2c inhibitor compounds in Applicants specification; 2) based on a combination of ordinary skill in the art as well as Applicants' disclosure of methods for determining 5-HT2c inhibition activity, find sufficient skill to make and determine 5-HT2c inhibitor compounds and prodrugs thereof; and 3) find predictability for methods of inhibiting 5-HT2c receptor (and disease mediated thereby) based on immutable showings of 5-HT2c inhibition activity of Applicants' compounds and uses thereof as demonstrated in the examples in Applicants' specification. In short, nowhere in the Action is evidence (other than conclusory assertions) provided that is contrary to that provided as written description in Applicants' specification.

Based on the foregoing, Applicants submit that the specification as filed enables one of ordinary skill to make and use the invention (i.e., prodrugs of the formula) and requests that this rejection be withdrawn.

(4) Disease States

It is alleged that Applicants provide no definitive evidence to correlate the many disease states being claimed from a reading of the specification. Applicants traverse. Applicants submit that one of ordinary skill in the art would, based on knowledge known to such a person at the time of filing as well as Applicants' specification, appreciate the correlation of the 5-HT_{2c} receptor and disease. Furthermore, it is alleged that because Gaster links 5-HT_{2c} antagonism to treatment of anxiety and depression, it is then concluded that Gaster evidences that the "level of skill in the art is not so high as to warrant treatment of all disease positively recited in the specification and embraced by the current claims." Applicants disagree with this overbroad conclusion.

Gaster does not provide support the conclusion in the Action, and even, *arguendo*, if one forwards that Gaster provides such support, that conclusion flies in the face of a multitude of literature (including that delineated below) that provides support for a correlation with the role of the 5-HT_{2c} receptor in therapeutic applications. Applicants submit the following correlative works, which exemplify support for the role of 5-HT_{2c} receptor in disease (while certain of the works in fact published after the filing date of the instant application, they evidence further verification of Applicants recitations in their specification as filed):

1. Schizophrenia:

(i) Piesla, M.J. et al. Atypical antipsychotic-like effects of 5-HT2C agonists. Schizophrenia Research 2001, 49 (1-2), 95. Sp. Iss. SI Suppl. (Appendix 4).

2. Pain:

(i) Murray, T.F. et al. A comparison of the analgesic activities of 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol (THIP) and 6-chloro-2[1-piperazinyl]pyrazine (MK 212). Eur. J. Pharmacol. 1983, 90 (2-3), 179-84 (Appendix 5; p. 184, last paragraph).

(ii) Chojnacka-Wojcik, E. et al. Involvement of 5-HT2C receptors in the m-CPP-induced antinociception in mice. Pol. J. Pharmacol. 1994, 46 (5), 423-8 (Appendix 6; abstract).

(iii) Solomon, R.E. et al. Mechanisms of effects of intrathecal serotonin on nociception and blood pressure in rats. J. Pharmacol. Exp. Ther. 1988, 245, 905-912 (Appendix 7; p. 911, 2nd last paragraph).

3. Substance Abuse:

(i) Rocha, B.A. et al. Enhanced locomotor, reinforcing, and neurochemical effects of cocaine in serotonin 5-hydroxytryptamine 2C receptor mutant mice. J. Neurosci. 2002, 22 (22), 10039-45 (Appendix 8; abstract, last sentence).

(ii) Tomkins, D.M. et al. An investigation of the role of 5-HT2C receptors in modifying ethanol self-administration behaviour. Pharmacol. Biochem. Behav. 2002, 71, 735-744 (Appendix 9; p. 743, 1st paragraph).

(iii) Grottick, A.J. et al. Studies to investigate the role of 5-HT2C receptors on cocaine- and food-maintained behaviour. J. Pharmacol. Exp. Ther. 2000, 295 (3), 1183-1191 (Appendix 10; p. 1190, last paragraph).

(iv) Grottick, A.J. et al. Activation of 5-HT2C receptors reduces the locomotor and rewarding effects of nicotine. Psychopharmacol. 2001, 157, 292-298 (Appendix 11; abstract, last sentence).

4. Urinary disorders:

(i) Steers, W.D. et al. Effects of serotonergic agonists on micturition and sexual function in the rat. Drug Dev. Res. 1992, 27, 361-375 (Appendix 12; p. 373, last paragraph).

(ii) Steers W.D. et al. Effects of m-chlorophenylpiperazine on penile and bladder function in rats. Am. J. Physiol. 1989, 257, R1441-R1449 (Appendix 13; p. R1448, last paragraph).

(iii) Guarneri, L. et al. The effects of m-CPP on bladder voiding contractions in rats are mediated by the 5-HT2A/5-HT2C receptors. Neurourol. Urodyn. 1996, 15, 316-317 (Appendix 14; last paragraph).

5. Memory disorders:

(i) Harvey, J.A. Serotonergic regulation of associative learning. Behav. Brain. Res. 1996, 73 (1-2), 47-50 (Appendix 15; p. 49, 1st paragraph).

(ii) Nitsch, R.M. et al. Serotonin 5-HT2a and 5-HT2c receptors stimulate amyloid precursor protein ectodomain secretion. J. Biol. Chem. 1996, 271(8), 4188-94 (Appendix 16; abstract).

(iii) Arjona, A.A. et al. Effect of a 5-HT(2C) serotonin agonist, dexnorfenfluramine, on amyloid precursor protein metabolism in guinea pigs. Brain Res. 2002, 951(1), 135-40 (Appendix 17; abstract, last sentence).

6. Sexual dysfunction:

(i) Bancila, M. et al. 5-Hydroxytryptamine 2C receptors on spinal neurons controlling penile erection in the rat. Neuroscience 1999, 92 (4), 1523-37 (Appendix 18; abstract, last paragraph).

(ii) Andersson, K.E. Pharmacology of penile erection. Pharmacol. Rev. 2001, 53(3), 417-50 (Appendix 19; p. 420, 2nd full paragraph, last sentence).

7. Anxiety disorders:

(i) Gaster, L.M. Annual Reports in Medicinal Chemistry, 1998, 33, 21-30 (Appendix 20, see p. 26, mid paragraph).

8. Mood disorders:

(i) Clenet, F. et al. Involvement of 5-HT(2C) receptors in the anti-immobility effects of antidepressants in the forced swimming test in mice. Eur. Neuropsychopharmacol. 2001, 11(2), 145-52 (Appendix 21, abstract).

(ii) Cryan, J.F. et al. Antidepressant-like behavioral effects mediated by 5-Hydroxytryptamine(2C) receptors. J. Pharmacol. Exp. Ther. 2000, 295 (3), 1120-6 (Appendix 22, abstract, last sentence).

9. Obesity

(i) Bickerdike, M. Diabetes, Obesity and Metabolism, 1, 1999, 207-214 (Appendix 3; abstract, last sentence).

Applicants submit that one of ordinary skill in the art (including those references recited above), taken in light of Applicants' specification and the disease states recited therein, would appreciate and understand how to make and use the methods and diseases of Applicants' claimed subject matter. No evidence is provide in the Action to support a contrary position. As such, Applicants request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-17 are rejected as unpatentable over Nilsson (WO '984) It is alleged in the Action that as Nilsson teaches saturated heteros both directly attached to phenyl but also indirectly attached with a C1-C6 alkylene, it would be obvious to replace morpholino with morpholinomethyl. Applicants traverse.

First, Applicants submit that the instant applciation is entitiled to priority benefit of the claimed priority applciations. Support for nitrogen-protecting groups appears at page 8, line 23 of US 60/253,702 and support for solvates appears at page 8, lines 6-10 as solvates are a form of prodrug. Furthermore, Applicants submit that based on the response above regarding enablement issues, Applicants are entitled to their priority claim for the same reasoning. Applicants submit that for the aforementioned reasons (see, sections regarding Rejections under 35 U.S.C. §112, above), Applicants are entitled to full priority benefit of their claimed prioirty applications SE 0004244-0 filed November 20, 2000 and U.S. provisional patent application no. 60/253,702, filed November 28, 2000. As such, WO '984 is not citable art and Applicants request withdrawal of this rejection.

Rejection under 35 U.S.C. § 103(a)

Claims 1-17 are rejected as obvious over Nilsson (US '467). Applicants, through their aforementioned representative, affirm that the instant application and US '467 were commonly owned (via assignment from the inventors) at the time the instant invention was made. As such, US '467 is disqualified as citable art under 35 U.S.C. § 103(a). Applicants therefore request withdrawal of this rejection.

Nonstatutory Double Patenting Objection

Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting. Upon disposition of the claims regarding the aformentioned rejections, a terminal disclaimer can be provided by Applicants.